# FACTORS PREDICTING EARLY GRAFT FUNCTION IN RENAL TRANSPLANTATION

*Dissertation submitted to*

**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**

***I**n partial fulfilment of requirements*

*For the award of the degree of*

**M.CH (UROLOGY) –BRANCH -IV**


**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**

**CHENNAI – TAMILNADU,INDIA**

**AUGUST 2014**

# DECLARATION

I solemnly declare that this dissertation entitled, **"FACTORS PREDICTING EARLY GRAFT FUNCTION IN RENAL TRANSPLANTATION"** is a bonafide work done by me in Department of Urology, Madras Medical College and Government General Hospital , under the guidance and supervision of the Professor **R.Jeyaraman, M.S,M.Ch(Uro).,** Professor and Head of Department, Department of Urology, Rajiv Gandhi Government General Hospital,Chennai.This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, in partial fulfillment of requirement for the award of Degreeof **M.Ch Urology.**

Place : DR.D.SHIVASHANKAR

Date :

# CERTIFICATE

This is to certify that the dissertation title **"FACTORS PREDICTING EARLY GRAFT FUNCTION IN RENAL TRANSPLANTATION"**submitted by DR.D.SHIVASHANKAR appearing for M.Ch(Urology) degree examination in August 2014 is a bonafide work done by him under my guidance and supervision in fulfilment of requirement of the Tamilnadu Dr. M.G.R. Medical University. I forward this to The Tamilnadu Dr. M.G.R. Medical University,Chennai.

**The Dean**
Madras Medical College,
Rajiv Gandhi Government
General Hospital,
Chennai – 600 003

**PROF.R.Jeyaraman,M.S.,M.Ch,**
Professor & Head of the Department,
Department of Urology,
Madras Medical College
Chennai - 600 003.

## ACKNOWLEDGEMENT

First of all,I thank all my patients for their cooperation, without whom this study would not have been possible.

I whole heartedly thank **The Dean**, Madras Medical College, and **Medical superintendent**,Rajiv Gandhi Government General Hospital, Chennai, for allowing me to avail the facilities needed for my dissertation work.

With extreme gratefulness, I express my indebtedness to **Prof.R.Jeyaraman,M.S.,M.Ch,**. Professor & Head of the Department, Department of Urology, Madras Medical College, for his expert guidance and help, rendered for the conduct and completion of my dissertation work.

I would like to thankfully acknowledge **Prof.V.Kamaraj M.S.,M.Ch**., and **Prof.RM.Meyyappan.M.S.,M.Ch**,Professors in Department of urology,for their constant help in carrying out my dissertation work.

I would extend my thanks to the Faculty, Department of Nephrology for their help and support.

I sincerely thank the Assistant Professors in the Department of Urology, for their continuous inspiration and support in carrying out my dissertation.

I thank my family members for their selfless support throughout my career.

Last, but not least, I thank my fellow postgraduates who helped me in carrying out my work and preparing this manual.

# INDEX

# INTRODUCTION

Renal transplantation is the treatment of choice for end stage renal disease , defined as glomerular filtration rate less than 15 ml /min/ 1.73 metre square body surface area . It is being increasingly offered for chronic kidney diseases with better creatinine clearance also , in view of its long term improvement of the quality of life .

There are two main types of renal transplantation , namely live renal transplantation and cadaver renal transplantation . Live renal transplantation is being done in many centres across india . However cadaver transplants are done in very few centres in the country . Our institute is one of the pioneers in doing cadaver renal transplants in the whole country . We have done around 130 cavdaveric transplantations so far and are the leading institute as far as cadaver transplantations are concerned . Our institute is also leading the way among government institutes in live renal transplantations with 989 transplantations done so far.

Transplantation is an example of multi- disciplinary team approach involving not only urologists and nephrologists, but also anaesthetists , neurosurgeons and pathologists working in concert to produce the best results for the patient .

Each recipient surgery is a study of the anatomy of the pelvis and each donor surgery is a study of retroperitoneal anatomy . Hence it requires considerable training and has a steep learning curve .

In spite of the being done with considerable surgical expertise and careful nephrological management , some cases of renal transplant recipients do not achieve the expected graft function in the long run . one such factor predicting the graft functioning in the long run is the estimation of early graft function at the end of the first week post transplant . in this study we have analysed the factors responsible for the early graft functioning of both live and cadaver renal transplants and the causes for delayed graft functioning .

## AIM OF THE STUDY

- To determine the factors predicting early graft function in both live and cadaver renal transplantations.

- To determine the factors responsible for delayed graft functioning .

# REVIEW OF LITERATURE

End stage renal disease is a cause of major morbidity as well as mortality world wide . Diabetes mellitus is the most common cause of ESRD, which is closely followed by systemic hypertension, chronic glomerulonephritis, and congenital cystic disease. India being the diabetes capital of the world has a significant chunk of renal failure cases of the world . There is a long waiting list for renal transplant recipients in india .

Each year hundreds of Indians die while waiting for an organ transplant. The reason: there is acute imbalance between the number of organs donated and the number of people waiting for a transplant. While 2.1 lakh Indians require kidney transplantation annually, but only 3000 – 4000 kidney transplants are done. The situation is not very different in relation to heart transplants. There are currently more than 120 transplant centres in India performing approximately 3,500 to 4,000 kidney transplants annually.

Organ donation and transplantation provides a second chance at life for thousands of people each year. The growing disparity between the rich and poor, demand for human organs and availability of technology in the country makes the organ trade a lucrative business opportunity for some and a source of relief for others who do not have a legitimate donor .

Donor selection

On the basis of preoperative evaluation , only those cases with normal preoperative creatinine clearance / GFR in whom nephrectomy will not affect the long term renal function are selected as donors . The basic criteria for a renal donor are an absence of any renal disorder with impaired function , an absence of focus of sepsis anywhere in the body , and absence of any active malignancy malignancy, especially if it is transmissible . as a policy always the better kidney is left back to the donor. This is done based on the preoperative evaluation of the GFR by isotope renogram studies . In females usually right kidney is selected , if the donor is in the reproductive age group because of the fact that both pyelonephritis of pregnancy and hydronephrosis are common on the right side than on the left .

Contradictions for choosing a prospective donor are psychiatric illness Already compromised renal function , significant comorbid medical illness especially cardiac, pulmonary illness, or diseases that can be transmitted to the recipient . ABO blood group incompatibility and a positive HLA crossmatch between the donor and the recipient are also considered as contraindications . Screening is done for diseases like HIV , Hepatitis B,C , cytomegalovirus and Epstein barr virus to prevent transmissible diseases .

Donor is also evaluated for diabetes by doing a random blood sugar and if the donor is a high risk candidate for diabetes then fasting and post prandial blood sugars or a glucose tolerance test are done as indicated.A screening usg is done to

look for any anomalies in the kidney like calculi , tumours and cysts . however the donor is usually screened with a CECT with a 3D reconstruction as well as CT angiogram to look for renal vascular anatomy and its variation regularly , thus making a screening ultrasound necessary only in centres where the CT is not done prior to surgery.

A cardiac evaluation is done routinely in some centres prior to transplantation to prevent major cardiovascular morbidity and mortality given the major nature of surgery . similarly BMI evaluation is also done prior to surgery and in some centres donors with a BMI > 32 % are excluded from donating . This is because of higher incidence of hyperfiltration injury in obese patients leading to progressive deterioration of renal function . it is for the same reason that advanced age group donors are not selected. Various centres have fixed cut off limits for age of the donor . usually it is kept at a maximum of 60 years if no other comorbid medical illness is present and the baseline GFR is > 90 ml/min . however in the presence of comorbid illness like hypertension or if the GFR is in the borderline of 80 – 90 ml/min then this age is reduced to 50 years. However it should be borne in mind that in the absence of no other prospective donors these criteria can be relaxed to certain extent .

The criteria for choosing a deceased donor are not much different and these include normal baseline renal function, absence of hypertension or diabetes .the

patient should no harbor a malignant tumor except for a non metatstatic brain tumor a superficial cancer of the skin which has been treated and cured .there should be no overwhelming Bacterial or viral infection , no gross abnormalities in the urinalysis , age should be between between six and fifty years, and serology should be negative for HIV, Hepatitis B,C , syphilis and CMV .

To overcome the donor shortage the expanded criteria for donors has been introduced , which includes age in the range between 50 – 60 years with any two of the three risk factors namely severe hypertension, cerebrovascular death and serum creatinine more than 1.5 mg/dl .

The cadaveric donor resuscitation is a very demanding procedure that requires trained intensivists in a ICU set up . the initial goal of resuscitation is to maintain a minimum systolic BP of more than 90 mm hg or a mean systolic BP of more than 60 mm hg. Equally important are the Monitoring of CVP , Pulmonary capillary wedge pressure for management of administration of fluids .

Serum electrolyte levels are monitored every 2 hourly . If the systolic BP cannot be maintained at adequate levels or if the CVP is persistently elevated then dopamine infusion can be given up to a maximum dose of 10 micro grams /min .this should be done very cautiously so as to not to reduce the renal perfusion.

Attempts are made to maintain a minimum hematocrit value of

25%, platelets more than 10,000/cu mm , INR should be less than 1.6 , fibrinogen greater than 100 ,core body temperature between 35° C to 37° C, and blood glucose in the range of 70 mg /dl to 110 mg/dL. Blood culture should be done if the donor has been admitted for more than 3 days .

Irrigation fluids

There are 2 methods for cold storage of the kidneys namely hypothermic irrigation followed by cold storage and pulsatile machine perfusion technique . the pulsatile machine perfusion uses a high protein solution and is not widely available . it is mainly used for the preservation of extended criteria donors in centres where the facilities are available . otherwise the most commonly used technique is cold storage after flushing with ice cold irrigation solution .

The commonly used irrigation solutions are university of Wisconsin solution , euro Collins solution and HTK or custodial solution . HTK solution is based on the principle of inactivating organ function by withdrawal of extracellular sodium and calcium, together with intensive buffering of the extracellular space by means of histidine/histidine hydrochloride, so as to prolong the period during which the organs will tolerate interruption of oxygenated blood. The composition of HTK is similar to that of extracellular fluid. All of the components of HTK occur naturally in the body.

HTK CONTENTS

| | |
|---|---|
| Sodium (mmol/L) | 15 |
| Potassium (mmol/L) | 9 |
| Magnesium (mmol/L) | 4 |
| Calcium (mmol/L) | 0.015 |
| Ketoglutarate/glutamic acid (mmol/L) | 1 |
| Histidine (mmol/L) | 198 |
| Mannitol (mmol/L) | 30 |
| Tryptophan (mmol/L) | 2 |
| Osmolarity (mOsm/L) | 310 |

The other irrigation solution most commonly used is university of Wisconsin solution. It contains high osmotic agents like Hydroxy Ethyl Starch , raffinose and lactobionic acid , which draw in fluid from the intracellular compartment and prevent cellular edema. Steroids and magnesium ions are used for membrane stabilizing properties . glutathione is used for its free radical scavenging effects . allopurinol for its inhibitory action on xanthine oxidase .

Finding a donor is the main issue in the country. Lack of awareness and improper infrastructure facilities are the main reasons behind the existing scenario. Administrative hurdles and conservative mindset further affect organ transplantation scenario in India. There are a lot of myths and fantasies associated with organ donation which needs to be addressed to solve this problem. Most Indians generally believe that it is against their religious belief to donate organs . Others believe that there might be a temptation to declare them dead before they are actually dead. Lack of a centralised registry for organ donation, acts as another major hurdle for the people to donate organs or get data about donors. Also, there is a problem of certifying brain deaths; if people are not aware of brain deaths, it becomes difficult to convince the relatives of the patients for organ donation.

Kidney transplants in India first started in the 1970s and since then India has been leading the asian continent in this field . The Government passed the Transplantation of Human Organ Act (THO) in 1994 which made unrelated transplants illegal and deceased donation a legal option with the acceptance of brain death. This was brought forward with the intent to reduce organ trade . however the concept of brain death has never been widely publicised and the layman is still in the dark , when it comes to the concept of brain death and organ transplantation. Unrelated transplants are now done only with the approval of an authorisation committee.

Government of India brought into force the 'Transplantation of Human Organs Act in the year 2011 which has simplified the organ transplantation act which was in force previously. The provisions included organ harvesting centres and their registration for the purpose of harvesting organs from cadaveric donours , donation by swapping and a compulsory inquiry by a medical officer of the concerned hospital along with the transplant coordinator concerned . The close relatives of the potential cadaver admitted in ICU are approached and explained about the option of organ donation in a way in which they can comprehend.

In India, the potential for deceased donation is huge due to the high number of major accidents in roads and this pool is yet to be tapped. At any given time, every major city has around 10 brain dead patients in various intensive care units . in india there are usually an estimated 1.5 lakh road traffic deaths occurring annually , and the actual incidence will be still higher as proper digital data recording systems are not widely employed everywhere. Out of these, almost two – thirds of the patients sustain severe head injuries , which means around ninety thousand people will be having a head injury .

Thus there is a tremendous opportunity to utilise this population of irreversible head injury patients for the purpose of cadaveric organ donation .While Spain has 35 organ donors per million people, Britain has 27 donors, US 26 and Australia 11, India's count stands at a mere 0.16 per million people.

This being one side of the problem , the other side is the durability of graft functioning in the long run . although live related transplants have a better long term graft function , the same cannot be said for cadaver transplants . Delayed graft function (DGF), defined as serum creatinine more than 1.5 mg /dl at the end of the first week or the need for dialysis in the first post transplant week occurs in 25

percent of the cadaver transplant cases .This incidence of delayed graft function also translates into poor long term graft function and is also an independent risk factor for both acute rejection as well as graft loss in the long term .

All the significant improvements in graft survival are seen only with respect to one year graft survival , but even now the rate of chronic graft loss after the one year remains somewhat high in spite of all the innovations made in the field of transplant surgery and the usage of novel immunosuppressive drugs .This is true for both live and cadaveric transplants and is higher for the latter. A 2005 study which was done to analyse renal transplants performed between the year 1995 and the year 2000 found that, despite a reduction in acute rejection rates, there was no improvement in the long term graft survival over the last decade. The only positive was the fact that the rate of decline in renal allograft function has some what slowed down in the last decade meaning that much better graft survival rates are possible in the near possible future .

Thus it is very important to have reliable predictive models to predict not only delayed graft function but also to predict the ultimate 10 year survival and

function of the renal allograft .many such models and nomograma have been published in the literature .

One study was done by ojo et al (1) studied the risk factors that lead to delayed graft function and its consequence on short term as well as the long-term graft survival. They studied the relationship between cold ischemia time and delayed graft function and overall long term renal transplant survival among 37,216 first time cadaveric renal transplants from the US renal data registry . then they analysed the

Relationships using both univariate and multivariate regression analysis models . in their study the duration of cold ischaemia was strongly associated with nonimmediate graft functioning as well as high rate of long term graft loss.they found out that the chance of delayed graft fuction was increased by almost 25 % for evary 6 hour delay in the anantamosis time . they also noted that Acute rejection occurred more commonly in patients with delayed graft function (36% vs. 21%; odds ratio=2.15, $P$=0.002). delayed grfat function was also a independent predictive variable for 5-year graft survival (relative risk=1.55, $P$<0.002). The combination of both an acute graft rejection and delayed graft function added up

to a very poor 5-year renal graft survival rate of only 34%.this was found to hold true in both univariate ana multivariate analysis. They also found out that a near zero percent HLA mismatch portended a better long term graft survival in the univariate analysis . however this was not significant in multivariate analysis and was thus not as significant as delayed graft function.

Delayed graft function is thus an independent predictor of both the short- and long-term renal allograft survival. Acute early rejection had a synergistic effect on long term graft survival. And more importantly the effect of delayed graft function is an even more important predictor of long term graft function than an HLA mismatch.

Another study by irish et al (2) including 19,706 cadaver transplants were obtained from the US renal data registry . they reported a high delayed graft function rate of around 24%. Sixteen independent variables , both donor and recipient were factors were found to be predictive of delayed graft function. They created a nomogram including the sixteen variables . This nomogram can be used to predict the risk of delayed graft function by adding the points for each independent variable .

Claudio jeldres et al later developed a simpler model to predict delayed graft function , to simplify the previous model which contained sixteen variables . the various predictive variables consisted of age of the transplant recipient ,the gender ,BMI , HLA major and minor mismatches, age of the donor and finally and most importantly cold ischemia time .

They found that age of the donor and BMI of the recipient and cod ischemia time were the independent predictors in logistic regression analysis and thus were highly predictive of delayed graft functioning in the recipient.

Recently parikh et al have developed bio markers for delayed graft function after transplantation. In this novel method they have used urinary neutrophil gelatinase-associated lipocalin (NGAL) and interleukin-18 (IL-18) as biomarkers for early identification of delayed graft functioning. However it is not a predictive tool but a biomarker for early idenfication of the subset of patients going for delayed function of graft . Both urine NGAL and IL-18 taken on the day of transplant were useful in predicting trend in serum creatinine in the first week post transplant in multivariate analysis.thus both NGAL and IL-18 can be used as sensitive tools to predict the delayed onset of graft functioning.

The various effects of donor kidneys on final outcome of graft functioning were analysed in a study by sita gourishankar et al . this was done by paired studying , which is nothing but  the extent to which two kidneys retrieved from the same cadaver donor tend to function in a similar manner.the function of one kidney taken from a cadaver donor will obviously predict the long term functioning of the other kidney as well.

# MATERIALS AND METHODS

## STUDY DESIGN

Prospective cross sectional  diagnostic study

## PLACE OF STUDY

The study was conducted in the Department of Urology, Madras Medical College and Rajiv Gandhi Government Hospital, Chennai- 3.

## ETHICAL CLEARANCE

The institutional ethical review board at our hospital approved the study.

## INCLUSION CRITERIA

All renal transplantation cases done between march 16 2013 to march 4 2014

## EXCLUSION CRITERIA

Patients with a failed previous transplantation.

## METHOD OF STUDY

Informed consent obtained from all the patients after explaining details of the study. All details were recorded in a proforma as an inpatient procedure. Analysis was done with the collected details prospectively.

## PATIENT EVALUATION

- Donor age , sex, BMI, comorbid illness, functioning status of the donor kidney ( renogram ) were collected.
- Recipient factors like age, sex, BMI, duration and severity of ESRD,associated bladder(cystogram) disorders will be collected
- Operative factors like perfusion time , cold ischemia time , type of perfusion solution, perfusion before versus after bench dissection, anastamosis time were noted

Other inadvertent factors like blood pressure fall, need for blood transfusion, vasopressor support were also recorded.

In this study we have analysed recipient factors which can cause a delyed graft functioning and mainly the factors responsible from the urological stand point were studied . age , sex, donor side , blood group match , cold ischemia time and hypotension if were all noted and recorded . then the patients were all followed up

in the post operative period and the serum creatinine at the end of the first week post transplant and /or the need for dialysis were all recorded.

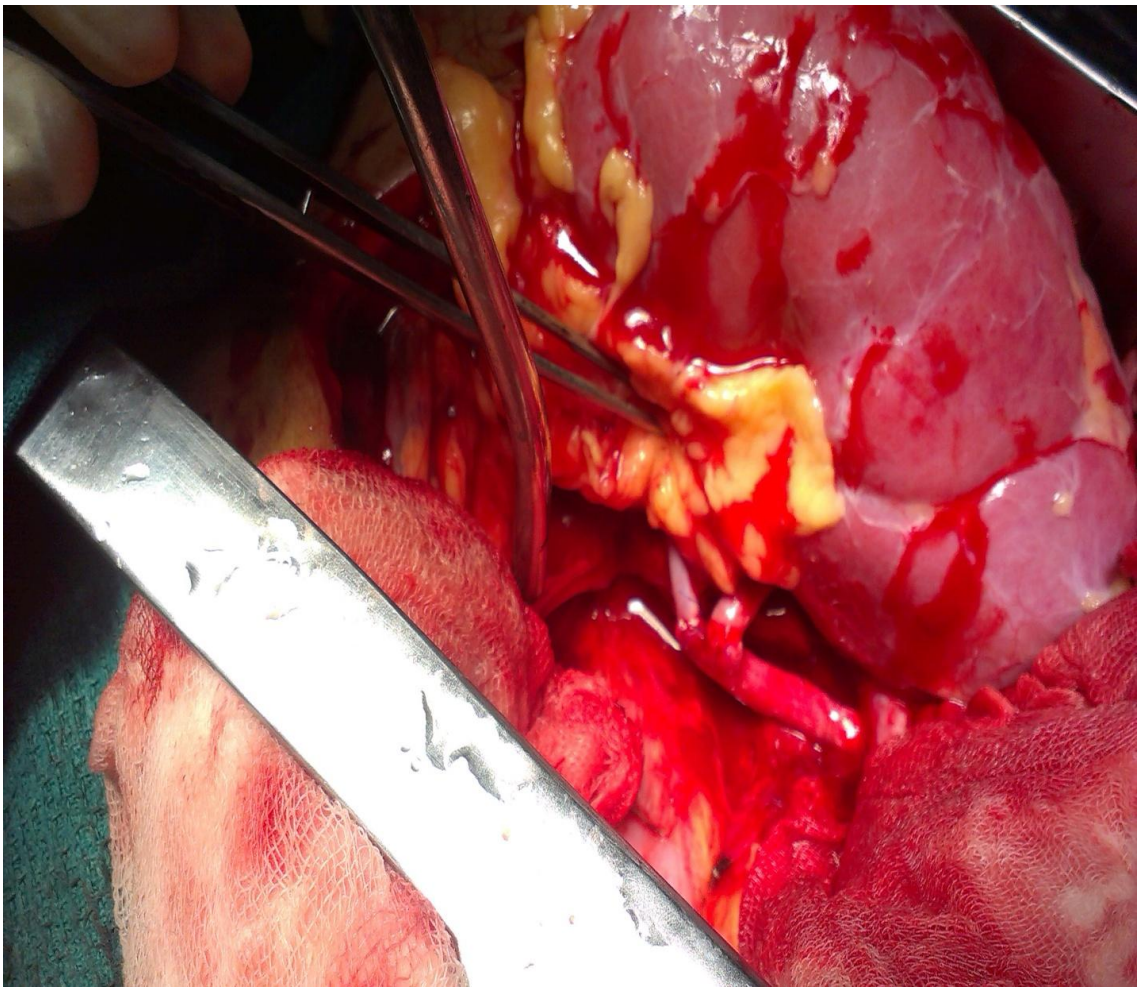
Investigation Details

Patient divided in to two groups (Group A&B) based on early versus delayed graft function . That is based on the presence or absence of delayed graft function .

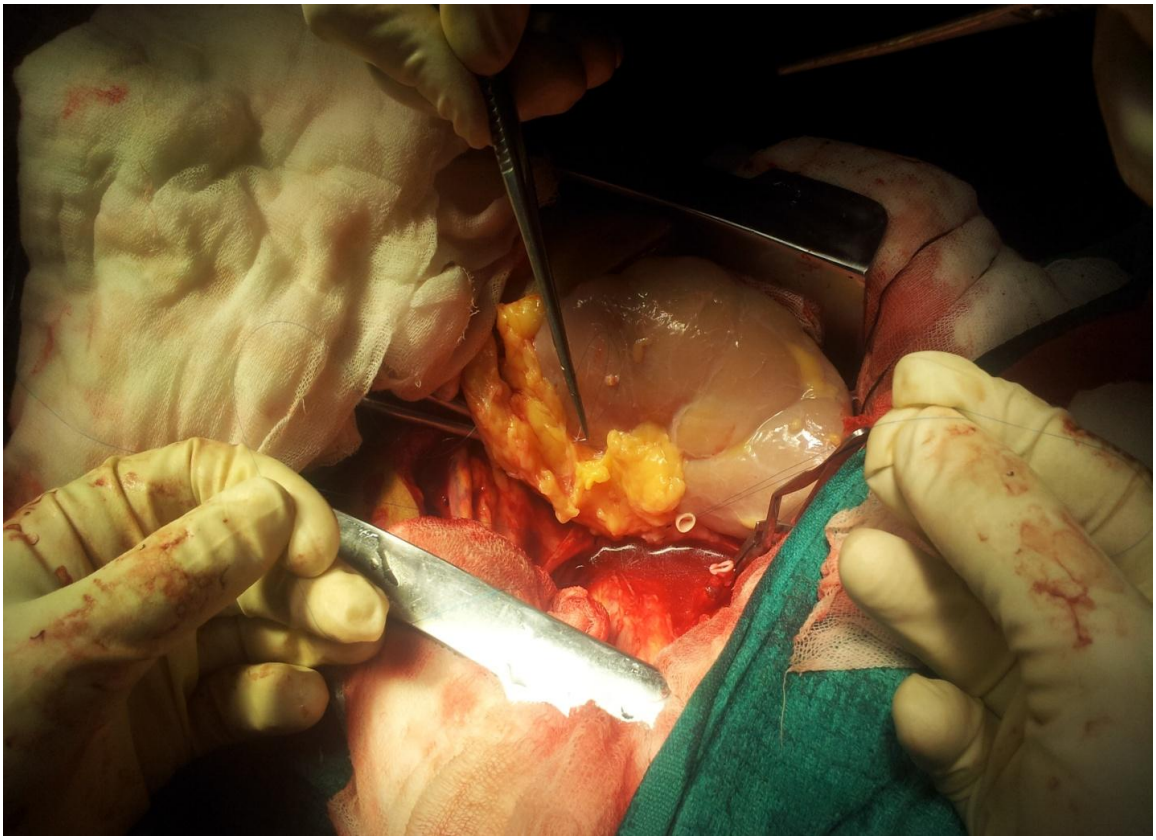
Data Collection and Methods

All patients will be followed both pre and post operatively

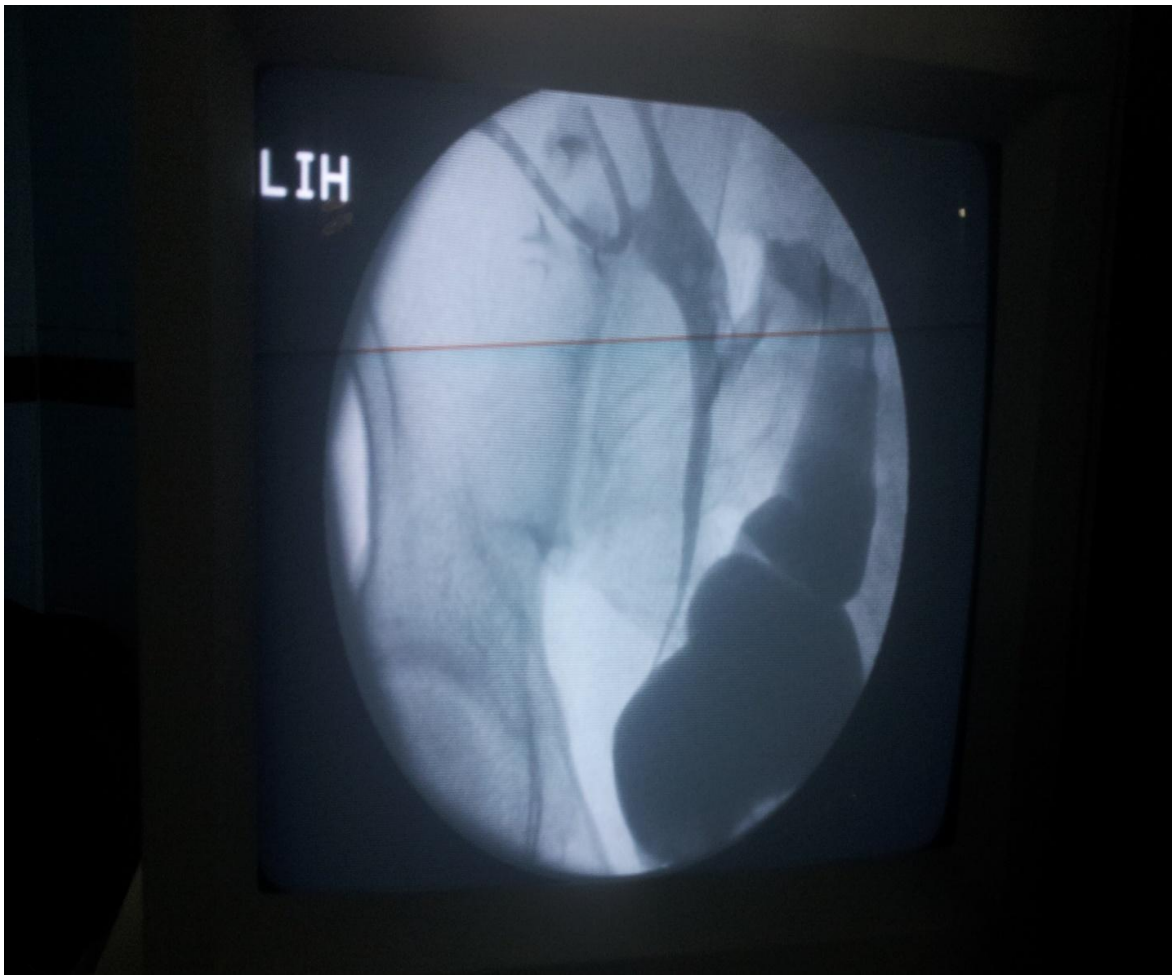
The data collected for analysis were the recipient age , sex , side , blood group match between donor and recipient, cold ischemic time and presence or absence of hypotension.Association was studied by using chi squared test to test the strength of association and a p value of $<0.05$ was considered as statistically significant.



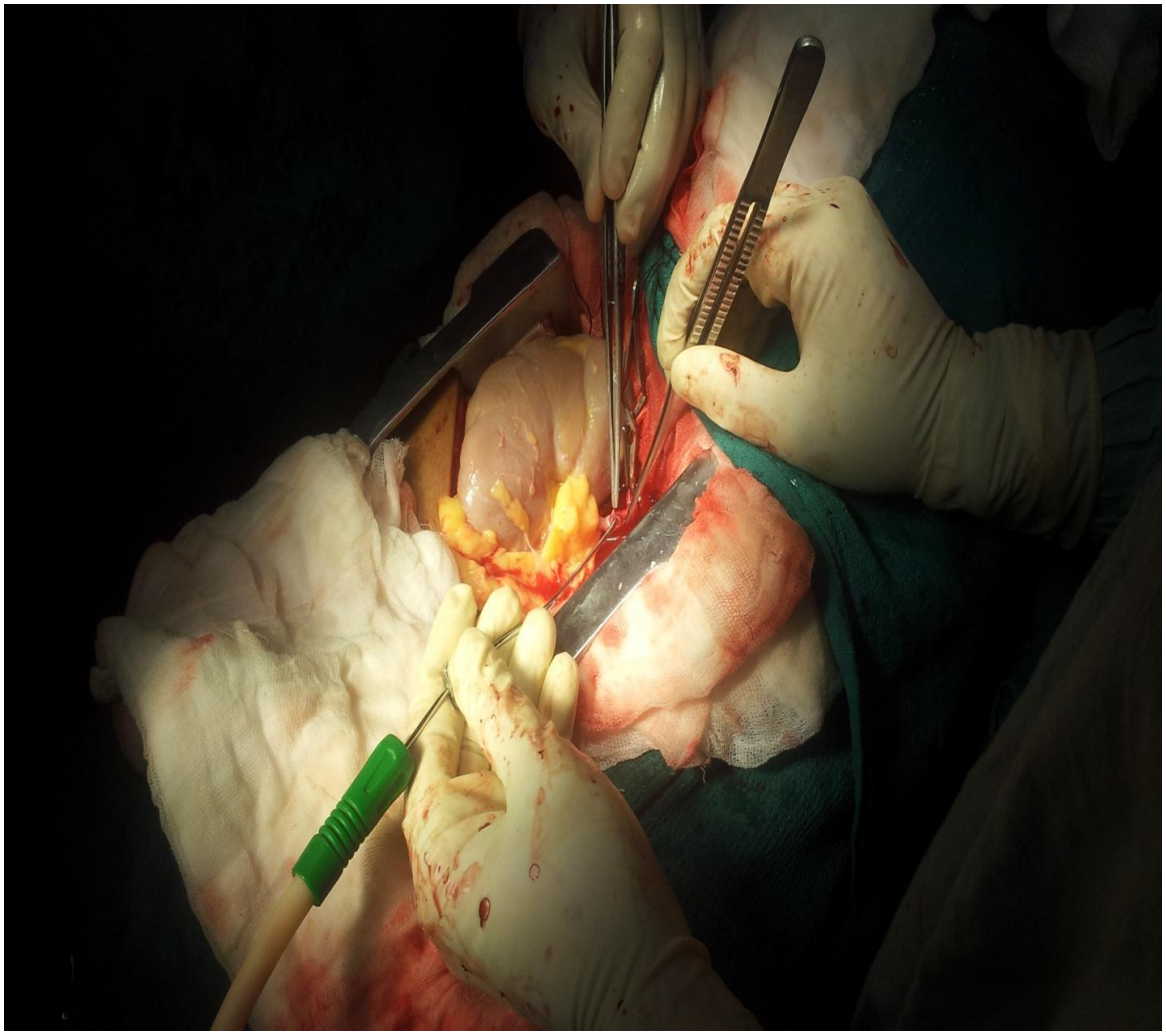
A case of double renal arterial anastamosis to internal iliac artery . the patient had no delay in graft functioning .



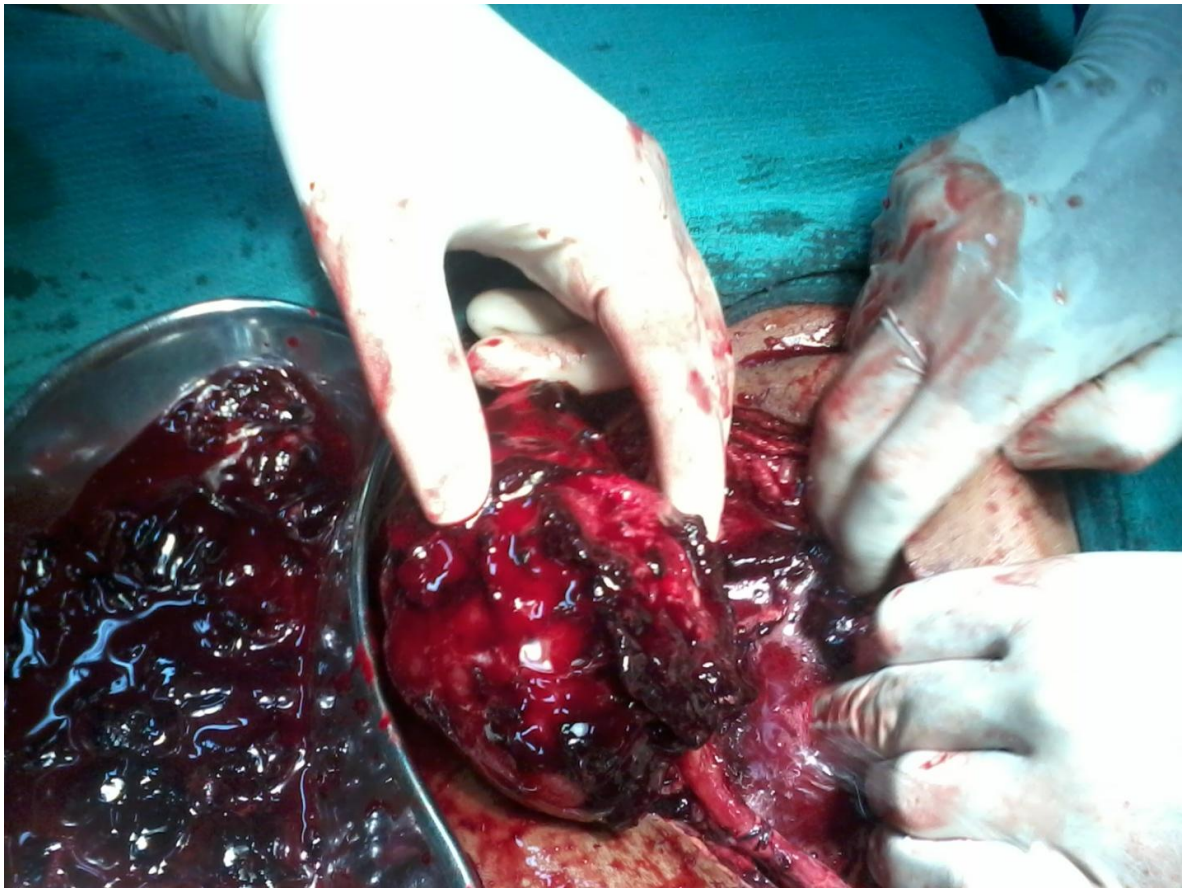
Recipient anastamosis between renal artery and internal iliac artery in an end to end fashion . we routinely perform end to end anastamosis between these 2 arteries . some centres also perfom end to side anastamosis between renal artery and external iliac artery.




An interesting case of post transplant recipient showing high grade reflux , due to inadequate evaluation prior to cadaver renal transplantation.



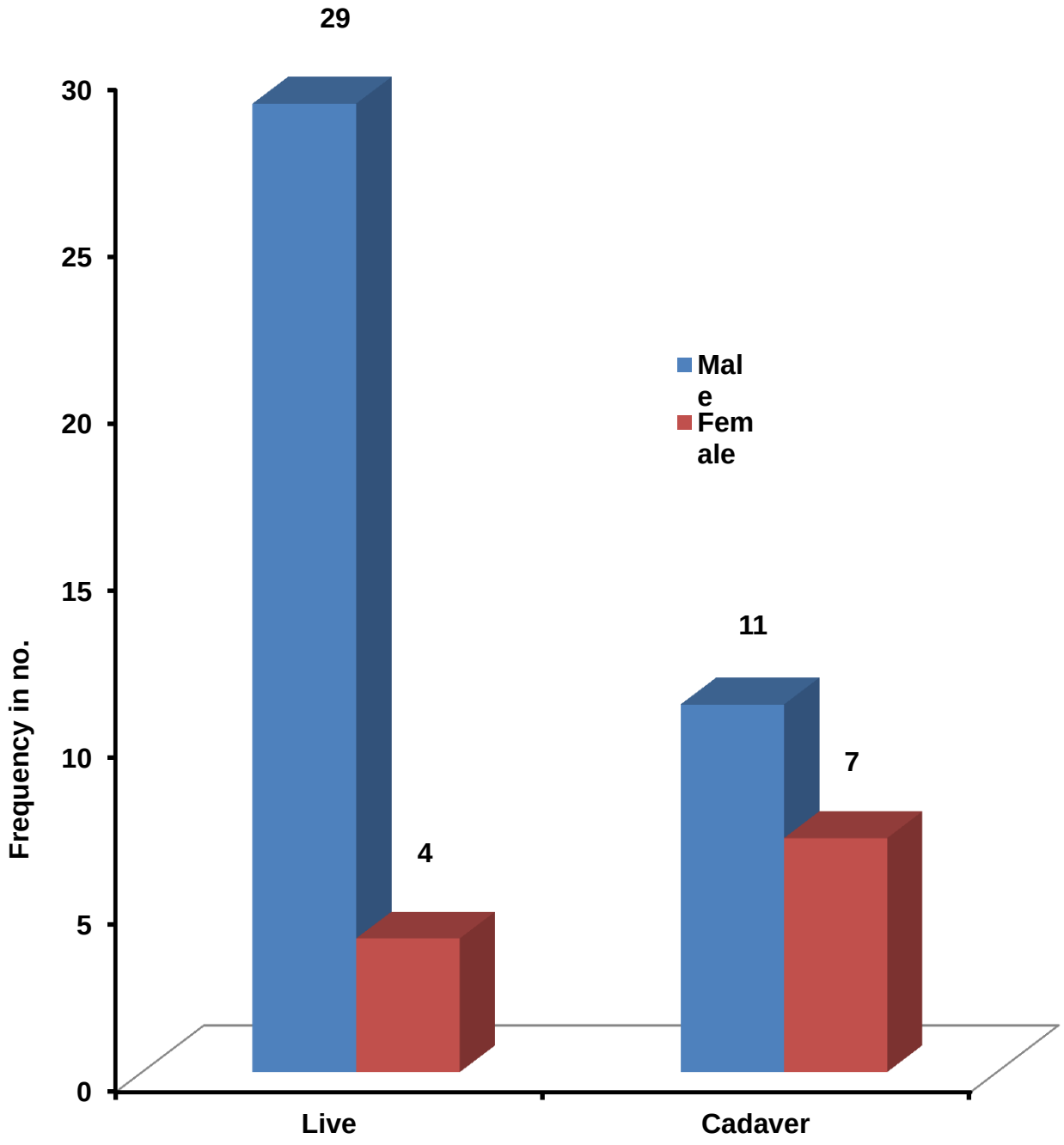
Arterial anastamosis in progress in  a cadaver transplant recipient.



Graft nephrectomy after graft rupture  a rare complication

# RESULTS

There was a total of 33 live cases and 19 cadaver transplant cases. The average age of the live transplant recipient was 31.5 with a SD of 11 and the average age of cadaver recipient was 34 with a SD of 10.1 . There was a higher proportion of male patients in the live group ,namely 29 out of 33 ,whereas in the cadaver group the proportion was less . it was only 11 out of 18 . there was ABO blood group mismatch in 8 out of the 33 live cases , but in onl;y 1 out of 17 cadaver cases. The majority of live donor kidneys were harvested from the left side but it was from the right side for the cadaver harvests.


29
30
25
20
15
10
5
0
Frequency in no.
Male
Female
11
7
4
Live
Cadaver

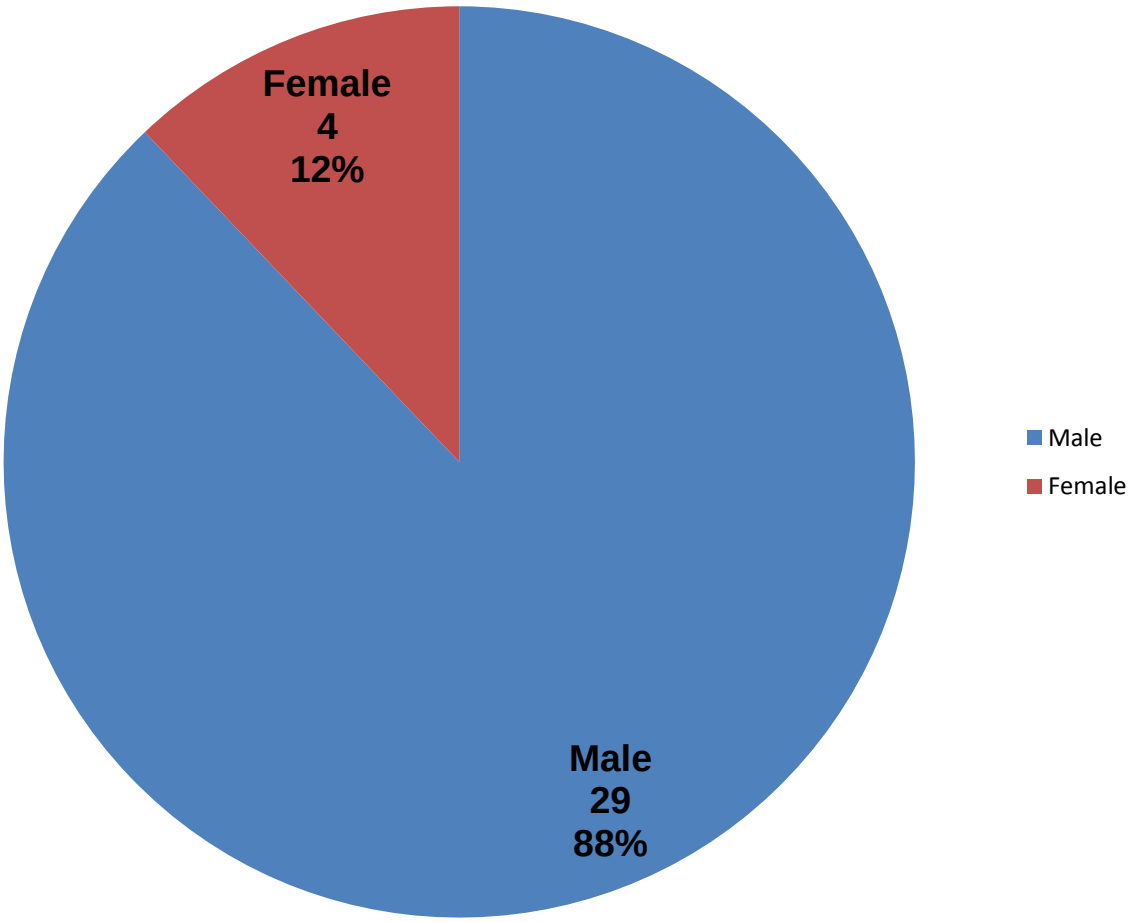
| | Live | Cadaver |
|---|---|---|
| Age | 31.5±11 | 34±10.1 |

| Sex | Live | Cadaver |
|---|---|---|
| Male | 29 | 11 |
| Female | 4 | 7 |

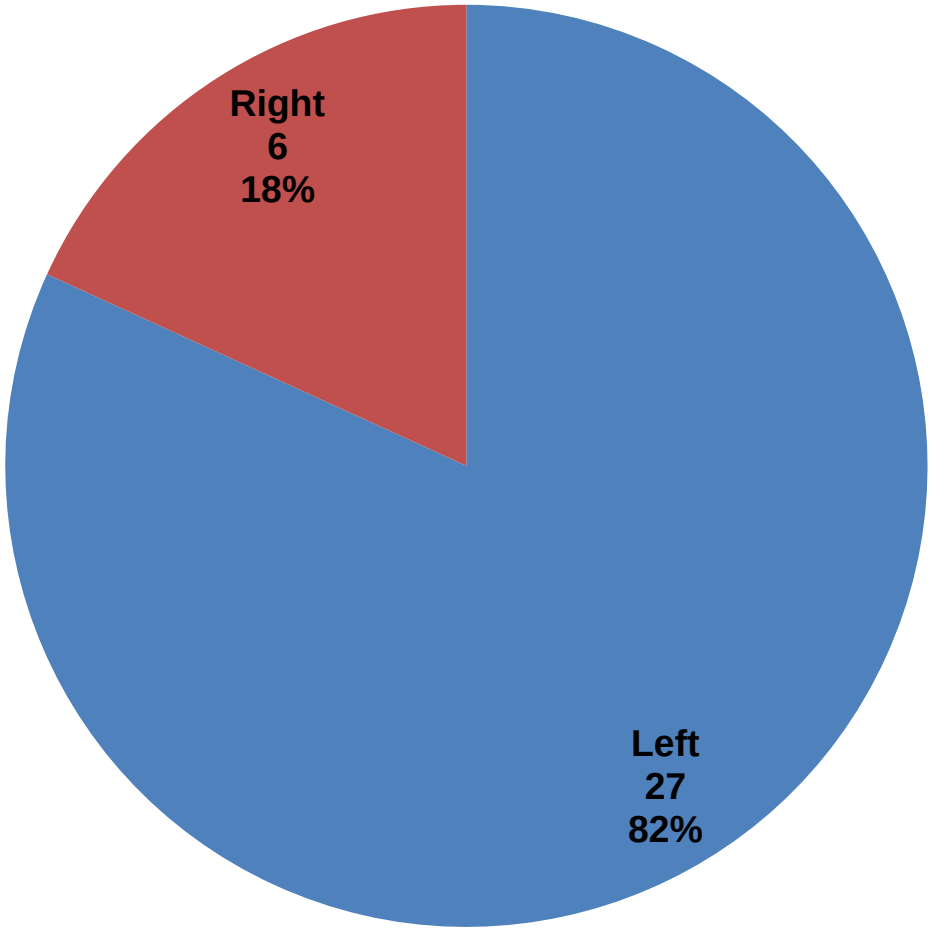
| Blood group | Live | Cadaver |
|---|---|---|
| Different | 8 | 1 |
| Same | 25 | 17 |

| Side | Live | Cadaver |
|---|---|---|
| Left | 27 | 8 |
| Right | 6 | 10 |

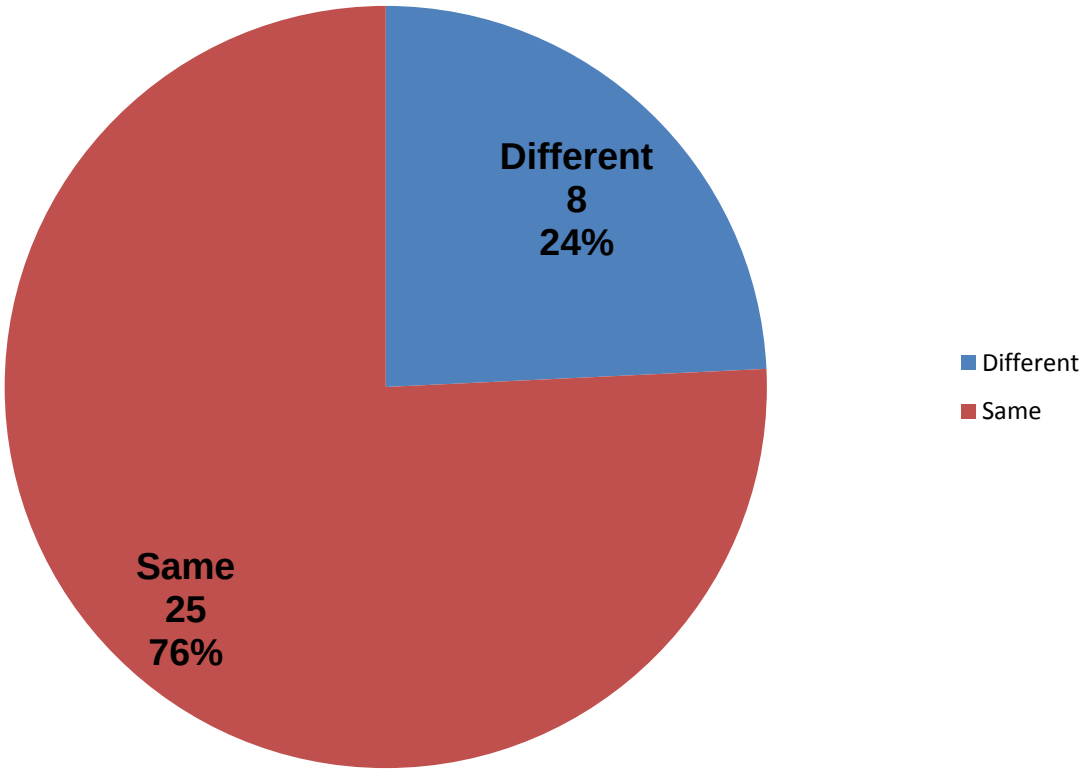
Among the live  cases there was a high preponderance of male cases.88 % of the cases were males and only 12% of the cases were females



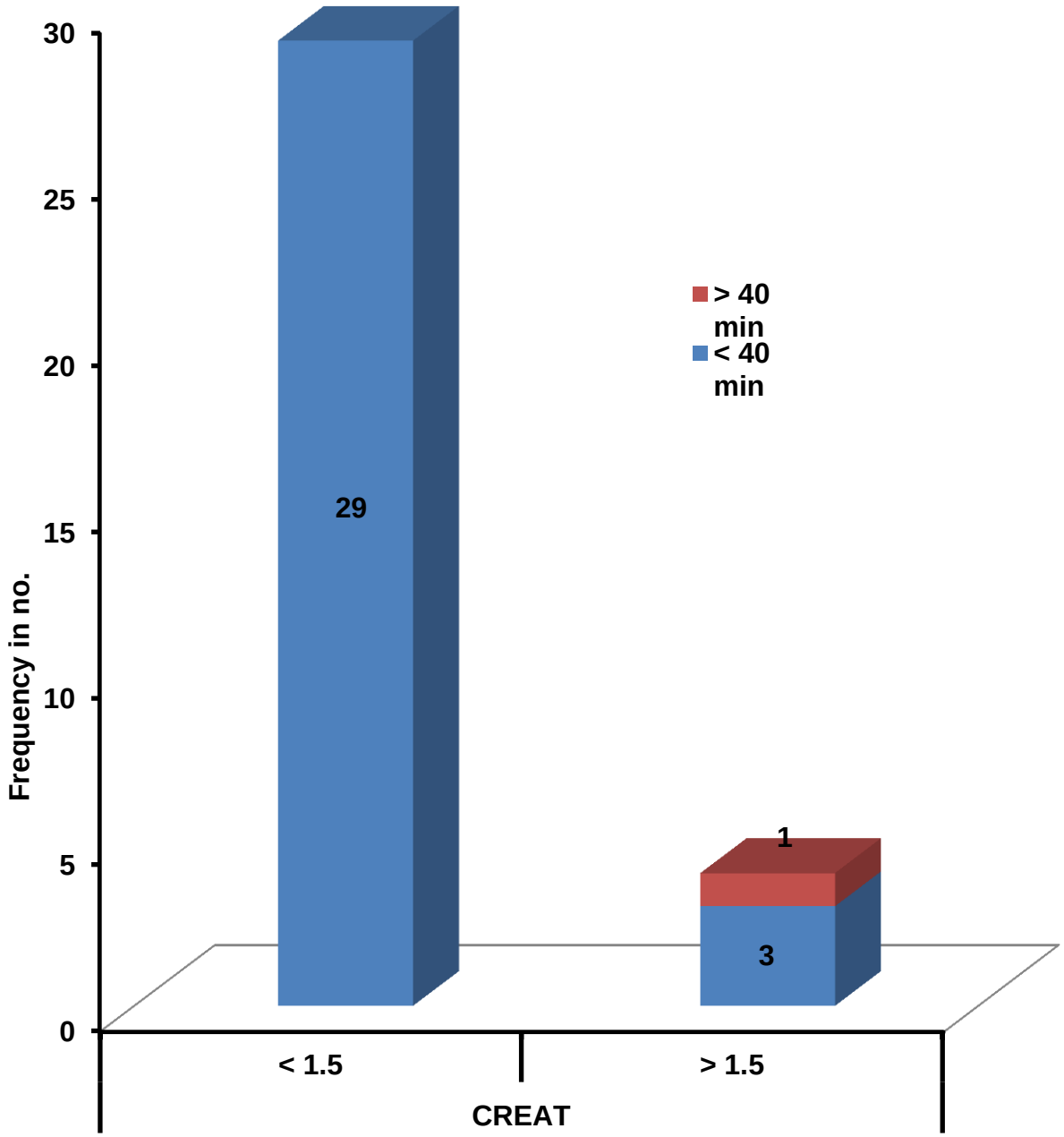
There was a predominance of left sided donors in the live group with 82 % of the donor kidneys were left sided and only 18% were from the right side



There was a blood group match in 76 % and ABO mismatch was present in only 24% of the cases



In the live group only 4 patients were having delayed graft function and needed dialysis in the immediate post operative period . out of the 4 cases , 1 had cold ischaemia time of >40 minutes . 3 of the 4 patients had an episode of intraoperative hypotension , out of which 3 were severe enough to require transfusion .1 patient expired in the first week post transplant due to refractory metabolic acidosis, inspite of dialysis. The following chart shows that prolonged cold ischemia was present in one out of four delayed graft function cases.

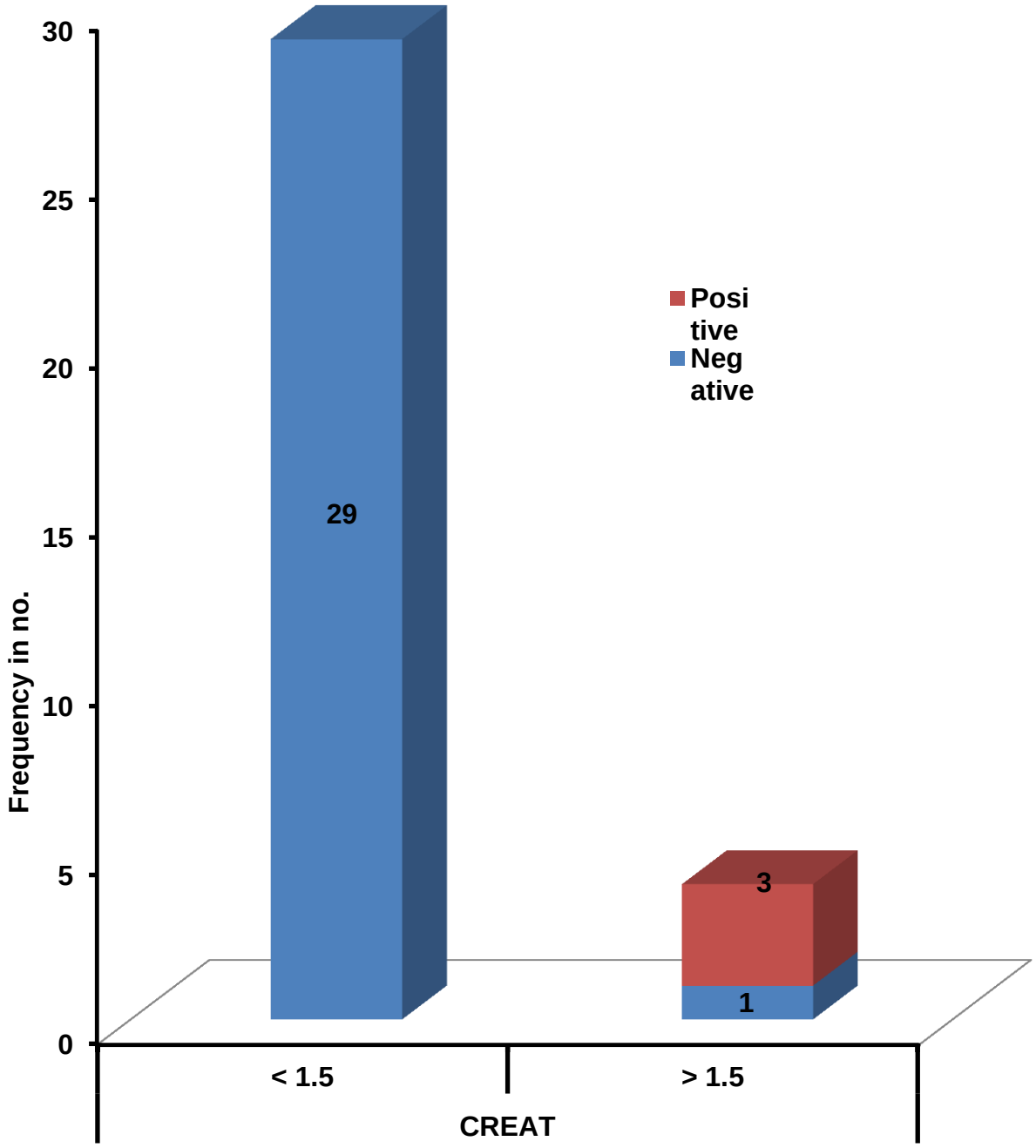

30
25
20
15
10
5
0
Frequency in no.
29
1
3
> 40 min
< 40 min
< 1.5
> 1.5
CREAT

The average cold ischemia time in the live group was 11.3 with 1 SD of 5.6 minutes

| **Live** | **CREAT** | | 1.1±0.3 |
|---|---|---|---|
| **COLD ISCH T** | **< 1.5** | **> 1.5** | |
| < 40 min | 29 | 3 | |
| > 40 min | | 1 | Chisquare |

P - value < 0.05

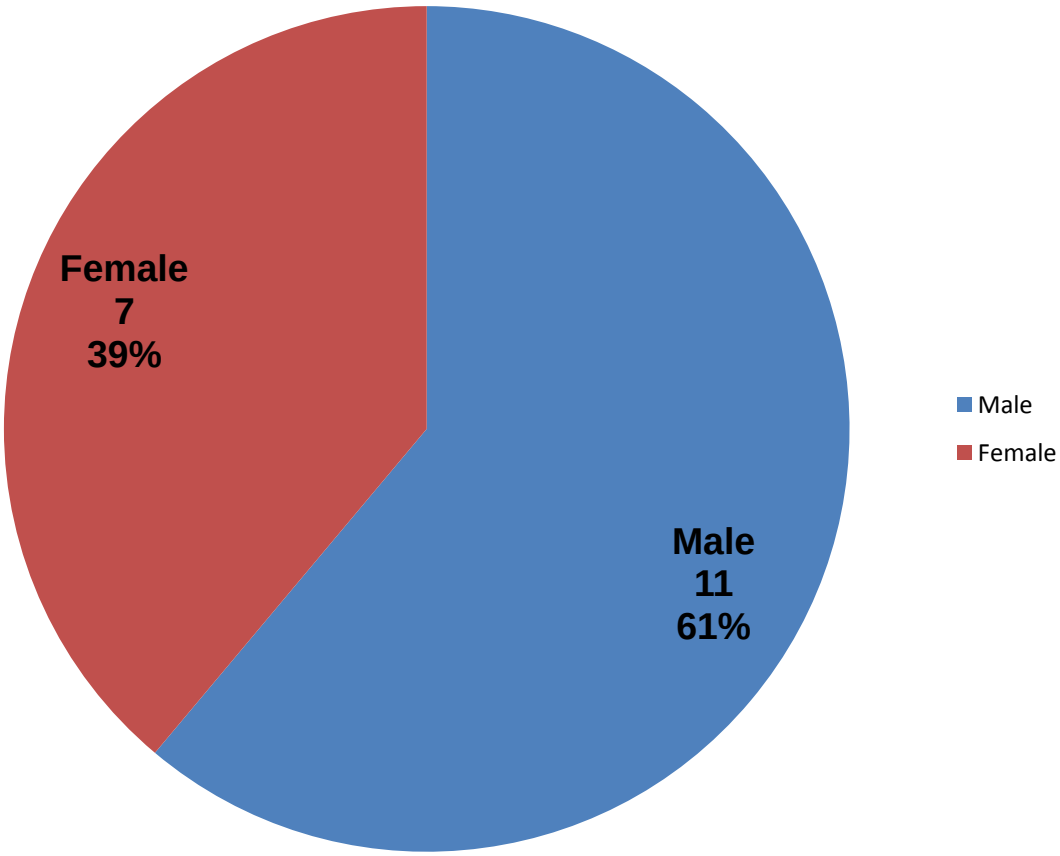
Average 11.3±5.6 min


30
25
20
15
10
5
0
Frequency in no.
29
3
1
Posi
tive
Neg
ative
< 1.5
> 1.5
CREAT

The above chart shows that significant hypotension was present in three out of four cases.

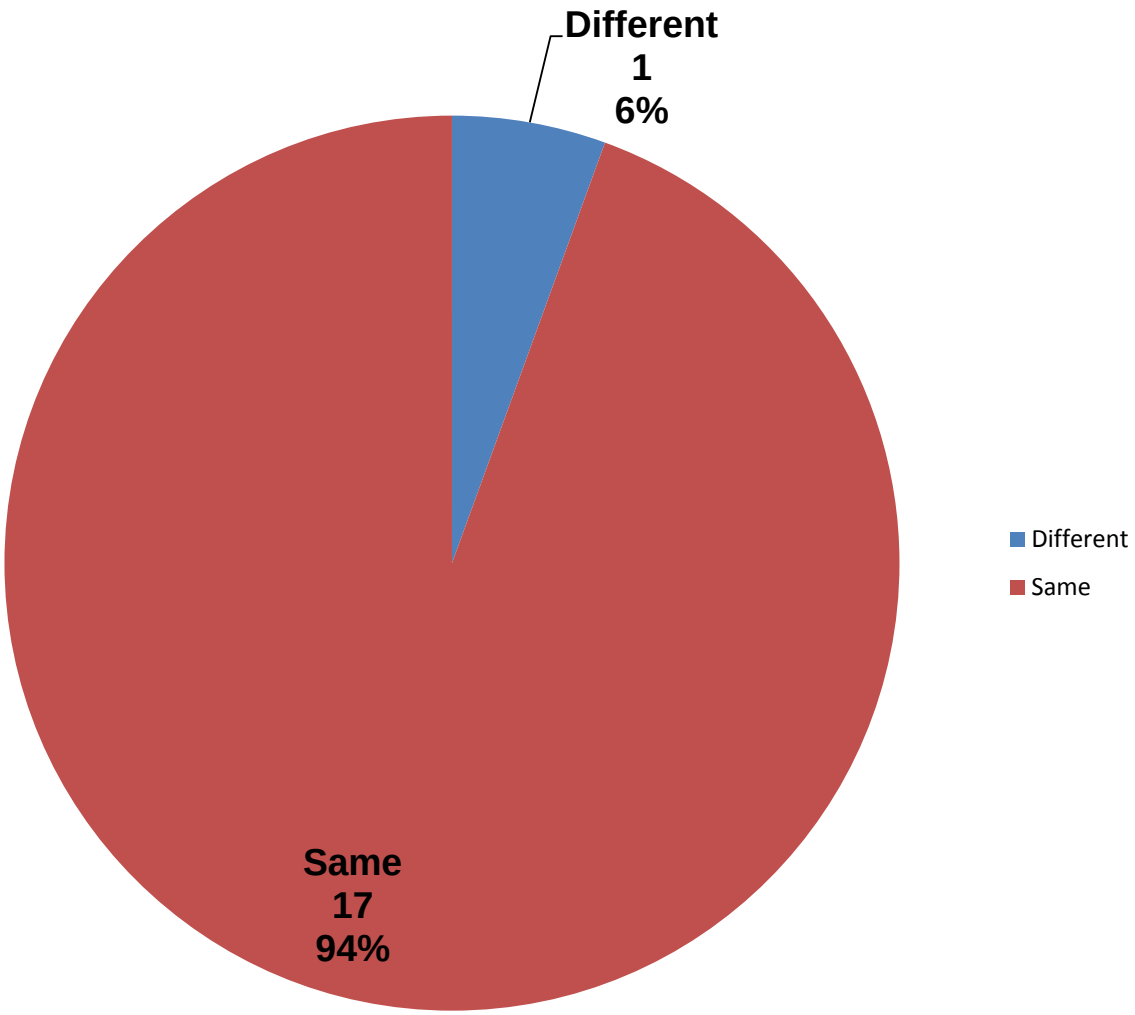
| **Live** | **CREAT** | | 2.1±1.02 |
|---|---|---|---|
| **HYPOTENSION** | **< 1.5** | **> 1.5** | |
| Negative | 29 | 1 | Chisquare |
| Positive | | 3 | |
| P - Value | < 0.001 | | |
| Average | 3±1.7 hrs | | |

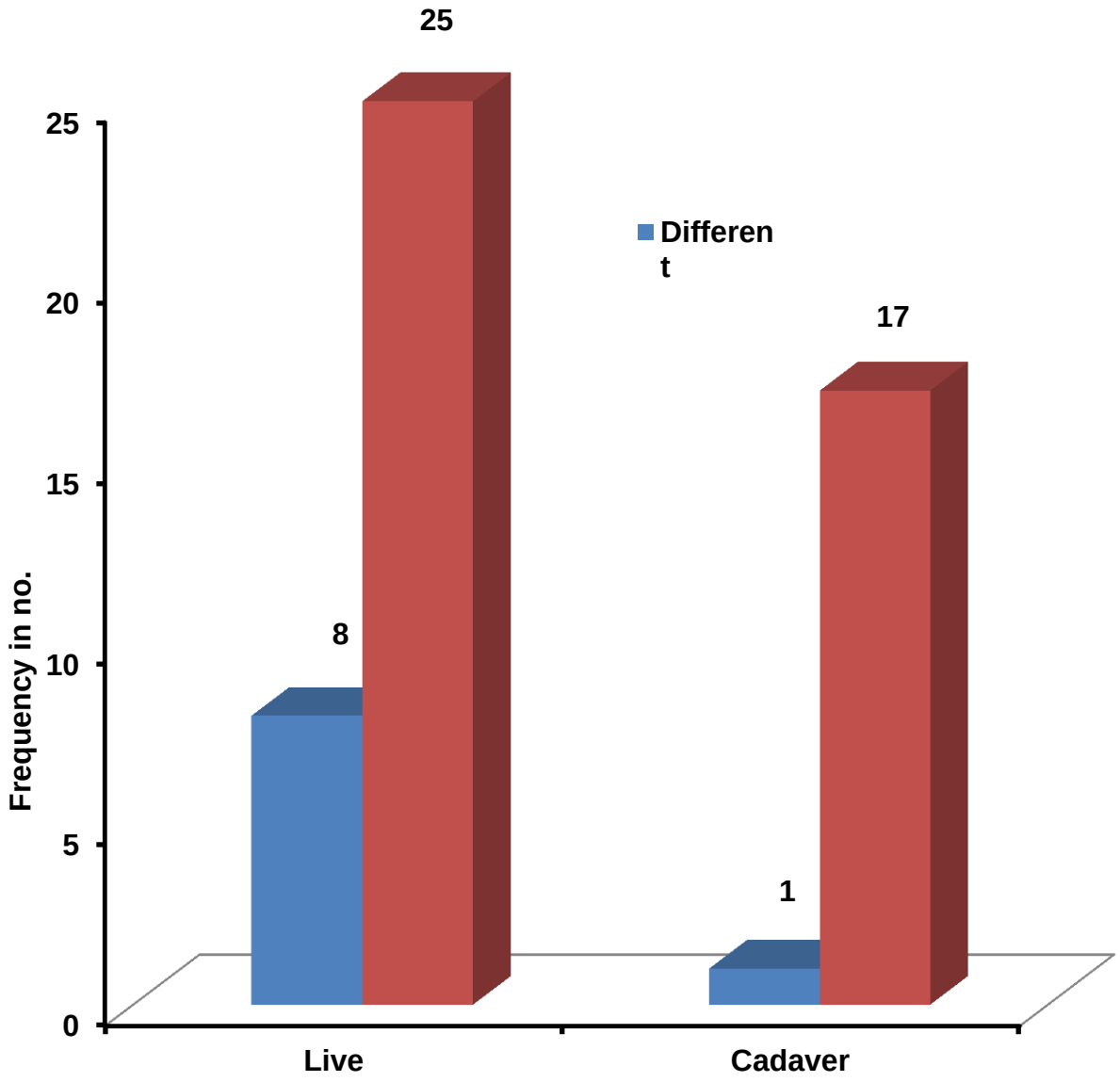
Among the cadaver transplants there were  11 males and 7 females accounting for 61% and 39% respectively .



Thus the male predominance was lesser in the cadaver transplant group compared to the live transplant group.

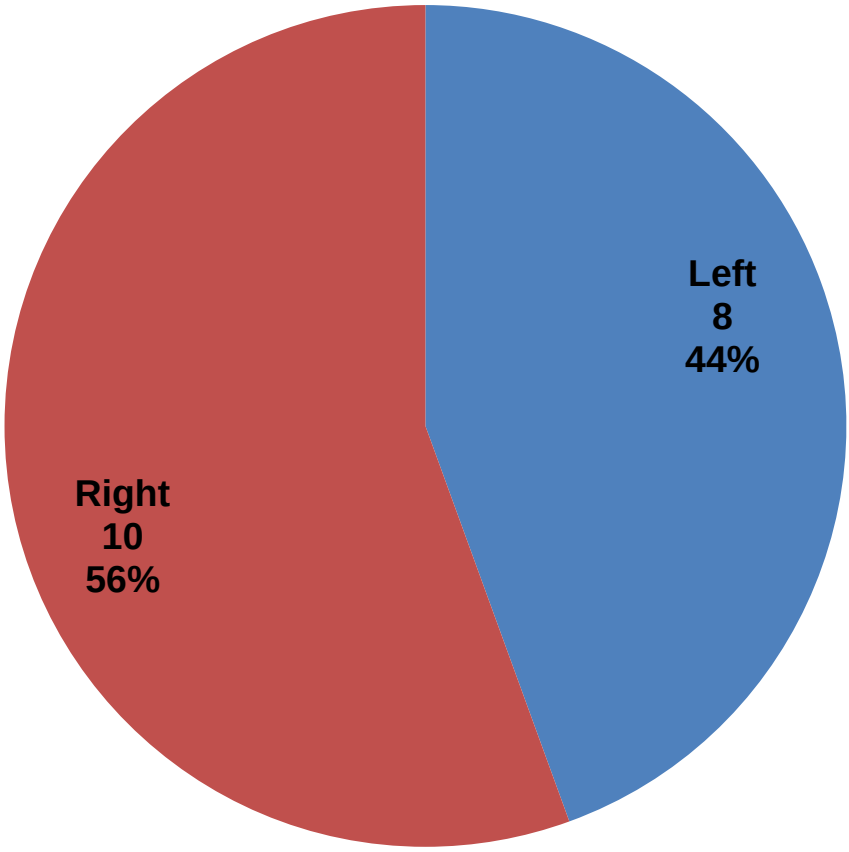
Blood group mismatch was only present in 1 out of the 18 cases. Thus blood group mismatch was very less in the cadaver transplant group .

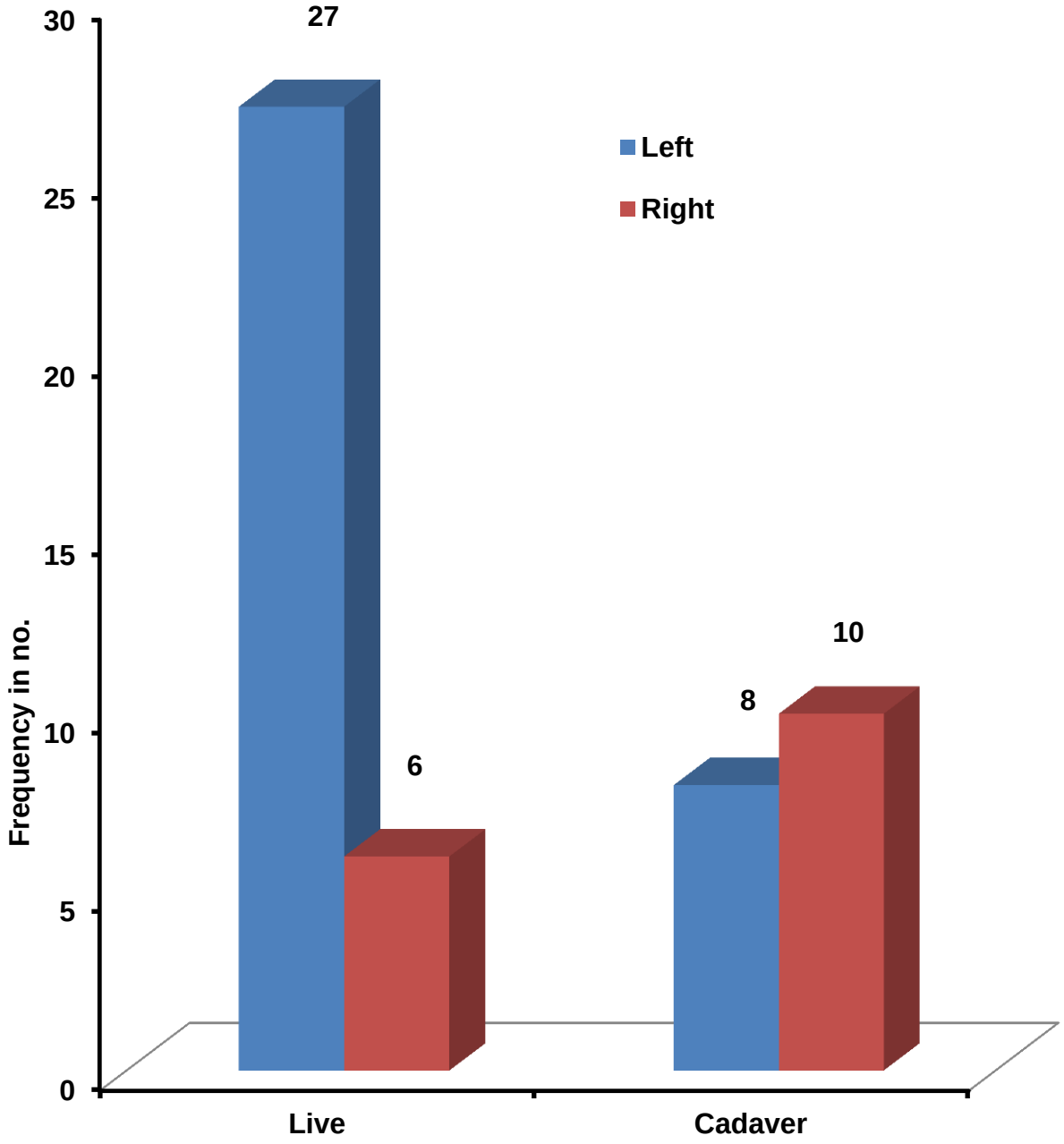





The above chart shows ABO mismatch rate in live and cadaver groups.

There was a predominance of right sided cadaveric donors , compared to the left sided predominance in live donors .




30
25
20
15
10
5
0
Frequency in no.
27
6
8
10
Left
Right
Live
Cadaver

The above chart shows this difference in side predominance between live and cadaver transplants.

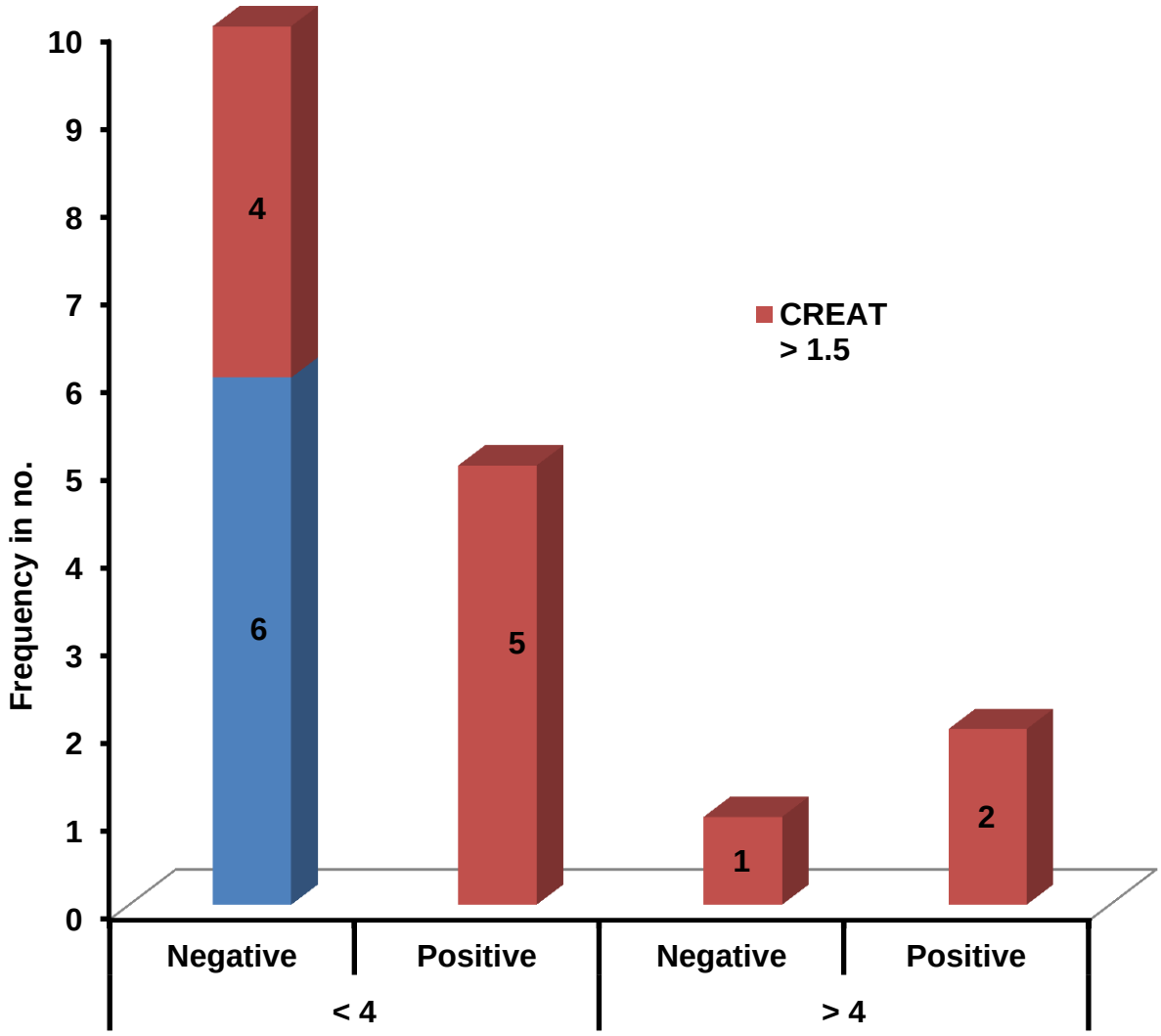
In the cadaver transplant group delayed graft function was present in 12 out of 18 patients . out of the 12, three patients had cold ischaemia time of more than 4 hours . nine of the patients had significant hypotension in the intraoperative period and there was also 4 deaths in this group .

| CADAVER | | CREAT | | Total |
|---|---|---|---|---|
| **COLD ISCH T** | **HYPOTENSION** | **< 1.5** | **> 1.5** | |
| **< 4** | **Negative** | 6 | 4 | 10 |
| | **Positive** | | 5 | 5 |
| **> 4** | **Negative** | | 1 | 1 |
| | **Positive** | | 2 | 2 |
| **Total** | | **6** | **12** | **18** |

Chisquare

P Value < 0.05

A bar chart showing the effect of cold ischemia time and hypotension in cadaver transplant group .



# DISCUSSION

Although many models to predict the delayed graft function are in use , there is no single simplified model to predict the onset of delayed graft functioning . Irish et al have proposed a nomogram model based on 16 independent variables to predict the onset of delayed graft function in the year 2003 . This was followed by a nomogram by Claudio et al in the year 2008 based on only six variables . however there are no studies looking at the factors responsible for delayed graft function from the urological stand point, especially in cadaver transplantation**.**

In this study we analysed three times in particular namely the warm ischemia time , cold ischemia time and the rewarming time. Warm ischemia time is the time from the ligation of the donor renal artery to the transfer of the kidney to the bench and onset of ice cold perfusion . cold ischemia time is the time from the onset of ice flush irrigation upto the point it is kept in cold storage . rewarming time is the time since the removal of the kidney from cold storage upto the point of reanastamosis and reestablishment of blood flow .In this study we only studied the cold ischemia time because the other two times were not much different in duration between live and cadaver transplantations.cold ischemia time was a predictor of delayed graft functioning , especially in cadaver transplant recipients . the mean cold ischemia time in the live group was 11.3 minutes where as in tha cadaver

group was 3.3 hours thus accounting for the significantly high incidence of delayed graft functioning in this group.

The other factor we studied in detail was the intraoperative hypotension severe enough to require transfusion. This factor is a significant predictor of delayed graft function in both live and cadaver transplant groups .in our study hyptension in the intraoperative period lead to not only delayed functioning of graft, but also to persistent post operative hypotension , refractory metabolic acidosis and even to death. This factor was a significant predictor of delayed graft function in both univariate and multivariate analysis .

The age of the patients in the live and cadaver transplant groups were not very much different . The cadaver group had a mean age of around 34 years where aa the mena age in the live group was slightly lower at 31 years . Although older studies show a correlation between increasing recipient age and incidence of graft loss ,it has been disproved in the recent study by cho et al . based on this study the maximal age limit for transplant recipient has been increased to upto 65 years in some high volume centres.

There is a clear cut sex divide between live and cadaver transplant groups in our centre , with 88 % of live transplants being males and only 1 2% being females . however this ratio is not the same in cadaver transplant recipients , with almost 40

% of the cadver transplant recipients being females . This might be due to the fact that in india , males being the breadwinners of the family in the majority of the cases, tend to get donors more easily than the females , who are dependent. This type of sex divide is not seen in data from developed countries .

Blood group mismatch was thought as a factor predicting rejection and thus delayed grfat function . however as shown by Gerald Lipshutz et al ABO incompatibility is not a adverse prognostic factor for the long term graft functioning . due to ever growing shortage of donor kidneys , they have suggested the following solutions for ABO incompatible cases. (1)transplantation across the

ABO blood group barrier, (2) transplantation across a positive crossmatch with desensitization,(3) paired exchange . in our study there was significant percentage of ABO mismatch in the live transplant group , but it did not adversely affect the graft functioning in the long run .

# CONCLUSION

In conclusion , our study shows that delayed graft functioning is a independent prognostic factor to predict the long term graft survival . It is an even more significant predictor of graft survival than HLA matching and thus achieving early graft function is of paramount importance .

In our study we found out that prolonged cold ischemia time and significant hypotension both independently can produce delayed graft function .Hence every effort should be made to reduce the duration of cold ischemia in cadaveric transplantations as well as to avoid significant hypotension.

Other factors like recipient age , gender , ABO mismatch , donor side were not significant predictors of delayed graft function

# BIBLIOGRAPHY


1) Ojo, Akinlolu O.[2]; Wolfe, Robert A.[3]; Held, Philip J.[2,3]; Port, Friedrich K.[2,3,4]; Schmouder, Robert L.[2,4,5] Transplantation: 15 April 1997 - Volume 63 - Issue 7 - pp 968-974 Clinical Transplantation

2) Irish WD[1], McCollum DA, Tesi RJ, Owen AB, Brennan DC, Bailly JE, Schnitzler MA. J Am Soc Nephrol. 2003 Nov;14(11):2967-74.

3) Claudio Jeldres, MD,[*] Héloïse Cardinal, MD,[†] Alain Duclos, MD,[*†] Shahrokh F. Shariat, MD,[*] Nazareno Suardi, MD,[*] Umberto Capitanio, MD,[*] Marie-Josèe Hébert, MD,[†] and Pierre I. Karakiewicz, MD, FRCSC Prediction of delayed graft function after renal transplantation

4) C. R. Parikh a, A. Jani J. Mishra Q.MaC. Kelly J. Barasch and P. Devarajan American Journal of Transplantation 2006; 6: 1639–1645 Blackwell Munksgaard

*5)* Donor Tissue Characteristics Influence Cadaver Kidney Transplant Function and Graft Survival but Not Rejection Sita Gourishankar*, Gian S. Jhangri†, Sandra M. Cockfield* and Philip F. Halloran* 10.1097/01.ASN.0000042164.03115.B8 *JASN February 1, 2003 vol. 14 no. 2 493-499*

6) Original Article Gerald S. Lipshutz, MD; Suzanne McGuire, RN; Qing Zhu, RN; Alyssa Ziman, MD; Rebecca Davis, MT(ASCP); Dennis Goldfinger, MD; Elaine F. Reed, PhD;

7) Alan H. Wilkinson, MD; ABO Blood Type–Incompatible Kidney Transplantation and Access to Organs

# INFORMED CONSENT FORM

**Title of the study:**

**“factors predicting early graft function in renal transplantation**

**Name of the Participant:**

**Name of the Principal Investigator :Dr.shivashankar.D**

**Name of theInstitution : Rajiv Gandhi Govt.General Hospital, Chennai -3.**

**Documentation of the informed consent**

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in **“factors predicting early graft function in renal transplantation”**

1. I have read and understood this consent form and the information provided to me.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past 3 months including any native (alternative) treatment.

6. I have been advised about the risks associated with my participation in this study.

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

8. I have not participated in any research study within the past 6 month(s)

10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

11. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.

12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

13. I have understand that my identity will be kept confidential if my data are publicly presented

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

**For adult participants:**

Name and signature / thumb impression of the participant (or legal representative if participantincompetent)

Name _____ Signature_____

Date_____

Name and Signature of impartial witness (required for illiterate patients):

Name _____ Signature_____
Date_____

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____
Date_____

# PROFORMA

**“A STUDY OF FACTORS PREDICTING EARLY GRAFT FUNCTION IN RENAL TRANSPLANT- DONOR**

- SL No. : Date :
- Patient name : Age/sex :
- IP .NO :
- Address :
- Past medical /surgical history :
- Personal history :
- Family history :
- General examination :
- Pulse : BP:
- P/A : E/G:

# INVESTIGATIONS

- HB
- TC
- DC

Urine R/E :

Urine C&S :

- ESR

- VIRAL MARKERS
- BLOOD GROUP

- RBS

- Blood urea

- Serum creatinine

- Serum Electrolytes

- USG KUB

- CT ANGIOGRAM

- ISOTOPE RENOGRAM

# PROFORMA

**"A STUDY OF FACTORS PREDICTING EARLY GRAFT FUNCTION IN RENAL TRANSPLANT – RECIPIENT**

- SL No. : Date :
- Patient name : Age/sex :
- IP .NO :
- Address :
- Chief complaints :
- Presenting illness :
- Past medical /surgical history :
- Personal history :
- Family history :
- General examination :
- Pulse : BP:
- P/A : E/G:

# INVESTIGATIONS

- HB
- TC
- DC

Urine R/E :

Urine C&S :

- ESR

- VIRAL MARKERS

- RBS

- Blood urea

- Serum creatinine

- Serum Electrolytes

- USG KUB

- CYSTOGRAM

# MASTER CHART

| SL NO | NAME | AGE/ SEX | IP NO | DOT | LIVE/CAD | IRR SOL/TIME | SIDE | COLD ISCH T | HYPOTENSION | BLD GP MATCH | CREAT |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | JANARTHANAN | 20/M | 27214 | 25.03.13 | LIVE | H+P | LT | 40MIN | NEGATIVE | SAME | 1.6 |
| 2 | ELUMALAI | 36/M | 27660 | 26.03.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | SAME | 0.9 |
| 3 | MOHANDOSS | 22/M | 28328 | 28.03.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | SAME | 0.9 |
| 4 | MANIMARAN | 34/M | 29860 | 04.04.13 | LIVE | H+P | LT | 7 MIN | NEGATIVE | SAME | 0.8 |
| 5 | ABDUL RASEED | 50/M | 33860 | 16.04.13 | LIVE | H+P | LT | 15 MIN | NEGATIVE | DIFF | 0.9 |
| 6 | PAULRAJ | 55/M | 37356 | 26.04.13 | LIVE | H+P | LT | 15 MIN | NEGATIVE | SAME | 0.8 |
| 7 | PARTHIBAN | 28/M | 38597 | 27.04.13 | LIVE | H+P | LT | 9 MIN | NEGATIVE | SAME | 0.9 |
| 8 | SELVAM | 30/M | 43285 | 14.05.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | SAME | 1.1 |
| 9 | RAJAVEL | 34/M | 46998 | 24.05.13 | LIVE | H+P | LT | 10 MIN | POSITIVE | SAME | EXP |
| 10 | RAJENDRAN | 28/M | 48109 | 28.05.13 | LIVE | H+P | RT | 15 MIN | NEGATIVE | SAME | 1.2 |
| 11 | SUSAIRAJ | 27/M | 55056 | 18.06.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | DIFF | 1.1 |
| 12 | DAMODHARAN | 32/M | 58805 | 27.06.13 | LIVE | H+P | LT | 10 MIN | POSITIVE | SAME | 1.9 |
| 13 | RAMESH | 32/M | 62496 | 09.07.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | SAME | 1 |
| 14 | RAVI | 45/M | 77197 | 20.08.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | DIFF | 1.1 |
| 15 | MINIMOL | 34/F | 79934 | 27.08.13 | LIVE | H+P | RT | 15 MIN | NEGATIVE | DIFF | 1.2 |
| 16 | SHEELA | 26/F | 87170 | 17.09.13 | LIVE | H+P | LT | 10 MIN | NEGATIVE | SAME | 1.2 |
| 17 | KARTHICK | 29/M | 89464 | 23.09.13 | LIVE | H+P | LT | 11 min | NEGATIVE | DIFF | 1.2 |
| 18 | SIVAGNANAM | 36/M | 89900 | 24.09.13 | LIVE | H+P | LT | 12 MIN | NEGATIVE | SAME | 1.1 |
| 19 | AYYAPPAN | 45/M | 91919 | 30.09.13 | LIVE | H+P | LT | 12 MIN | NEGATIVE | SAME | 1.1 |
| 20 | MANIVASAN | 15/M | 95305 | 08.10.13 | LIVE | H+P | LT | 5 MIN | NEGATIVE | SAME | 1 |
| 21 | ILAYARAJA | 32/M | 99943 | 22.10.13 | LIVE | H+P | RT | 12 MIN | NEGATIVE | SAME | 0.9 |
| 22 | KARTHIKEYAN | 26/M | 1E+05 | 28.10.13 | LIVE | H+P | LT | 11 MIN | NEGATIVE | SAME | 0.9 |
| 23 | GAYATHRI | 21/F | 1E+05 | 12.11.13 | LIVE | H+P | LT | 12 MIN | POSITIVE | SAME | 1.9 |
| 24 | SHEIKFARID | 17/M | 1E+05 | 22.11.13 | LIVE | H+P | LT | 7 MIN | NEGATIVE | SAME | 0.8 |
| 25 | RAMAKRISHNAN | 20/M | 1E+05 | 06.12.13 | LIVE | H+P | LT | 7 MIN | NEGATIVE | SAME | 0.8 |
| 26 | VELMURUGAN | 55/M | 1E+05 | 17.12.13 | LIVE | H+P | RT | 8 MIN | NEGATIVE | DIFF | 1.5 |
| 27 | SETTU | 46/M | 1E+05 | 20.12.13 | LIVE | H+P | LT | 9 MIN | NEGATIVE | DIFF | 1.2 |
| 28 | SRIMATHI | 23/F | 3054 | 10.01.14 | LIVE | H+P | RT | 10 MIN | NEGATIVE | SAME | 1.2 |
| 29 | SHEKAR | 45/M | 4070 | 13.01.14 | LIVE | H+P | RT | 9 MIN | NEGATIVE | SAME | 1.1 |
| 30 | MUNUSAMY | 37/M | 8518 | 27.01.14 | LIVE | H+P | LT | 10 MIN | NEGATIVE | DIFF | 1.2 |
| 31 | VENKATACHALAM | 27/M | 12503 | 07.02.14 | LIVE | H+P | LT | 11 MIN | NEGATIVE | SAME | 1.1 |
| 32 | DILLIGANESH | 18/M | 13103 | 10.02.14 | LIVE | H+P | LT | 12 MIN | NEGATIVE | SAME | 0.9 |
| 33 | ARAVINDKUMAR | 16/M | 12256 | 24.02.14 | LIVE | H+P | LT | 11 MIN | NEGATIVE | SAME | 0.9 |

| SL NO | NAME | AGE/ SEX | IP NO | DOT | LIVE/CAD | IRR SOL/TIME | SIDE | COLD ISCH T | HYPOTENSION | BLD GP MATCH | CREAT |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | SHIVAKUMAR | 31/M | 24697 | 16.03.13 | CADAVER | CUSTODIAL | LT | 2 HRS | NEGATIVE | SAME | 1.5 |
| 2 | ELANGO | 42/M | 24716 | 17.03.13 | CADAVER | H+P | RT | 3 HRS | POSITIVE | SAME | 3.3 |
| 3 | RAJI | 32/M | 25944 | 20.03.13 | CADAVER | CUSTODIAL | RT | 4 HRS | NEGATIVE | SAME | 4.1 |
| 4 | ASLAM BASHA | 24/M | 30145 | 02.04.13 | CADAVER | H+P | RT | 6 HRS | NEGATIVE | SAME | 2.5 |
| 5 | HEMAVATHI | 24/F | 32254 | 09.04.13 | CADAVER | CUSTODIAL | LT | 1 HR | NEGATIVE | SAME | 1.1 |
| 6 | NILOFER | 35/F | 37510 | 25.04.13 | CADAVER | CUSTODIAL | RT | 3 HRS | NEGATIVE | SAME | 1.9 |
| 7 | DEVI | 27/F | 39886 | 01.05.13 | CADAVER | H+P | RT | 6 HRS | POSITIVE | SAME | EXP |
| 8 | ELANGOVAN | 43/M | 51592 | 05.06.13 | CADAVER | CUSTODIAL | LT | 1 HR | NEGATIVE | SAME | 1.1 |
| 9 | JANAKI | 40/F | 54865 | 14.06.13 | CADAVER | H+P | RT | 3 HRS | POSITIVE | SAME | 4.1 |
| 10 | RAJESWARI | 47/F | 55378 | 17.06.13 | CADAVER | H+P | RT | 2 HRS | POSITIVE | SAME | EXP |
| 11 | MANJU PRIYA | 17/F | 69313 | 26.07.13 | CADAVER | H+P | LT | 3 HRS | POSITIVE | SAME | 2.1 |
| 12 | NAWASKHAN | 26/M | 67346 | 26.07.13 | CADAVER | H+P | RT | 2 HRS | NEGATIVE | SAME | 1.5 |
| 13 | AMBIKESWARI | 46/F | 86979 | 15.09.13 | CADAVER | H+P | LT |  | POSITIVE | DIFF | EXP |
| 14 | RAJAN | 30/M | 87263 | 16.09.13 | CADAVER | CUSTODIAL | LT | 4 HRS | NEGATIVE | SAME | 1.5 |
| 15 | SRINIVASAN | 28/M | 87251 | 16.09.13 | CADAVER | CUSTODIAL | RT | 1 HR | POSITIVE | SAME | EXP |
| 16 | VELLAISAMY | 56/M | 95969 | 09.10.13 | CADAVER | CUSTODIAL | LT | 1 HR | NEGATIVE | SAME | 1.3 |
| 17 | NAGARAJAN | 38/M | 95971 | 09.10.13 | CADAVER | CUSTODIAL | RT | 4 HRS | NEGATIVE | SAME | 1.6 |
| 18 | SYEDALI | 26/M | 1E+05 | 29.12.13 | CADAVER | H+P | LT | 3 HRS | NEGATIVE | SAME | 1.9 |

# ஆராய்ச்சி ஒப்புதல் படிவம்

## ஆராய்ச்சி தலைப்பு

**சிறுநீரக ஒட்டுசெடி செயல்திறனை பாதிக்கும் காரணிகள் பற்றிய ஓர் ஆராய்ச்சி**

| | | | |
|---|---|---|---|
| பெயர் | : | தேதி | : |
| வயது | : | உள் நோயாளி எண் | : |
| பால் | : | ஆராய்ச்சி சேர்க்கை எண் | : |

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் நான் பங்கு பெறுகின்றேன். இந்த ஆராய்ச்சியில் இருந்து நான் எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

இந்த ஆராய்ச்சியினால் ஏற்படும் நன்மைகளையும் சில பக்க விளைவுகளையும் பற்றி தெளிவாக மருத்துவர் மூலம் தெரிந்துகொண்டேன்.

நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள் :
இடம் :

# ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜீவ்காந்தி அரசு பொது மருத்துவனையில் சிறுநீரக ஒட்டுசெடி செயல்திறனை பாதிக்கும் காரணிகள் பற்றிய ஓர் ஆராய்ச்சி இங்கு நடைபெறுகிறது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் உங்களுடைய இரத்தம், சிறுநீர் மற்றும் ஸ்கேன் ஆகியவற்றை சிறப்பு பரிசோதனைக்கு உட்படுத்தி அதன் தகவல்களை ஆராய்வோம். அதனால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்பு ஏற்படாது என்பதையும் தெரிவித்துக்கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்பு சிகிச்சையின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

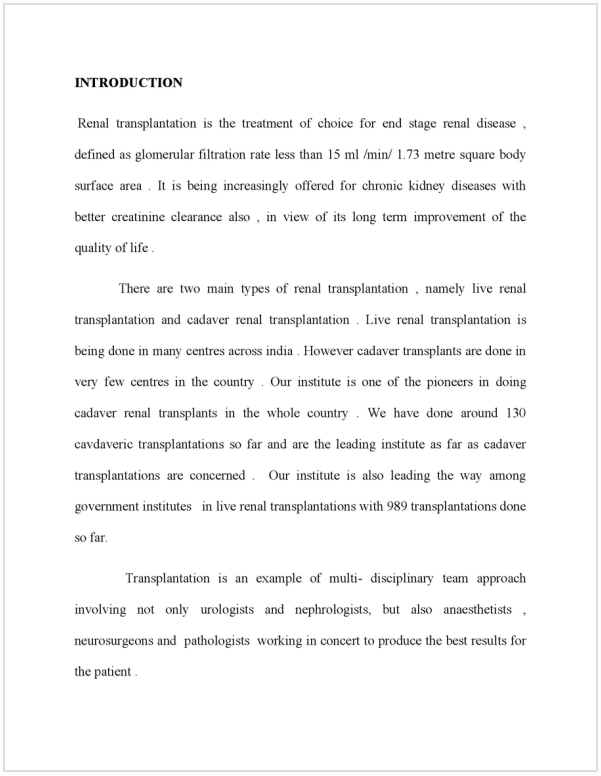
நாள் :
இடம் :

# Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

| | |
|---|---|
| Submission author: | 18112508 . M.ch. Urology SHIVASHANKAR DAMODARAN |
| Assignment title: | Medical |
| Submission title: | factors predicting early graft functioning in renal transplantation |
| File name: | transplant_thesis.docx |
| File size: | 1.99M |
| Page count: | 51 |
| Word count: | 4,887 |
| Character count: | 24,645 |
| Submission date: | 28-Mar-2014 09:19PM |
| Submission ID: | 410653131 |



**INTRODUCTION**

Renal transplantation is the treatment of choice for end stage renal disease , defined as glomerular filtration rate less than 15 ml /min/ 1.73 metre square body surface area . It is being increasingly offered for chronic kidney diseases with better creatinine clearance also , in view of its long term improvement of the quality of life .

There are two main types of renal transplantation , namely live renal transplantation and cadaver renal transplantation . Live renal transplantation is being done in many centres across india . However cadaver transplants are done in very few centres in the country . Our institute is one of the pioneers in doing cadaver renal transplants in the whole country . We have done around 130 cavdaveric transplantations so far and are the leading institute as far as cadaver transplantations are concerned . Our institute is also leading the way among government institutes in live renal transplantations with 989 transplantations done so far.

Transplantation is an example of multi- disciplinary team approach involving not only urologists and nephrologists, but also anaesthetists , neurosurgeons and pathologists working in concert to produce the best results for the patient .

Turnitin Originality Report
factors predicting early graft functioning in renal transplantation by 18112508 . M.ch. Urology SHIVASHANKAR DAMODARAN
From Medical (The Tamil Nadu Dr. M.G.R. Medical University)

- Processed on 28-Mar-2014 23:44 IST
- ID: 410653131
- Word Count: 4887

Similarity Index
19%
Similarity by Source
Internet Sources:
11%
Publications:
12%
Student Papers:
2%

**sources:**

**1**

7% match (Internet from 19-Feb-2014)
http://rosemaryinstitute.com/essayarticles/2062-article-organ-donation-and-transplantation-provides-second-life-to-thousands-of-people

**2**

2% match (Internet from 04-Jan-2011)
http://medlibrary.org/medwiki/Histidine-tryptophan-ketoglutarate

**3**

2% match (publications)
"AMERICAN TRANSPLANT CONGRESS 2012 ABSTRACTS", American Journal of Transplantation, 05/2012

**4**

1% match (publications)
"American Transplant Congress 2007 Executive and Program Planning Committees and Abstract Review Committees", American Journal of Transplantation, 5/2007

**5**

1% match (publications)
"WORLD TRANSPLANT CONGRESS 2006 ORAL ABSTRACTS", American Journal of Transplantation, 8/2006

**6**

1% match (publications)
Akinlolu O. Ojo. "DELAYED GRAFT FUNCTION: RISK FACTORS AND IMPLICATIONS FOR RENAL ALLOGRAFT SURVIVAL1", Transplantation, 04/1997

**7**

1% match (publications)
"Abstracts 544 - 1089", American Journal of Transplantation, 3/2004

**8**

1% match (publications)
C. R. Parikh. "Urine NGAL and IL-18 are Predictive Biomarkers for Delayed Graft Function Following Kidney Transplantation.", American Journal of Transplantation, 7/2006

**9**